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(FILE 'HOME' ENTERED AT 16:33:03 ON 08 JUL 2005)

FILE 'REGISTRY' ENTERED AT 16:33:10 ON 08 JUL 2005

L1 492 TKPPR/SQSP

L2 4890 ?PHOSPHOLIP?/CNS

FILE 'HCAPLUS' ENTERED AT 16:33:55 ON 08 JUL 2005

L3 - 274 L1

L4 59589 L2

L5 QUE PHOSPHOLIPIDS+OLD, NT/CT

L6 7858 L4-5 (L) (CONJUGAT? OR LINK? OR RACT+NT/RL)

L7 2 L3 AND L6

FILE 'HCAOLD' ENTERED AT 16:35:03 ON 08 JUL 2005

FILE 'USPATFULL, USPAT2' ENTERED AT 16:35:22 ON 08 JUL 2005

FILE 'HCAOLD' ENTERED AT 16:36:57 ON 08 JUL 2005 0 L1 AND L2

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L8

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FILE COVERS 1907 - 8 Jul 2005 VOL 143 ISS 3 FILE LAST UPDATED: 7 Jul 2005 (20050707/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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- L7 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2002:778699 HCAPLUS
- DN 137:299916
- ED Entered STN: 11 Oct 2002
- TI Peptide-containing compounds for targeting cells expressing NP-1 receptor
- IN Von Wronski, Mathew A.; Marinelli, Edmund R.; Nunn, Adrian D.; Pillai, Radhakrishna; Ramalingam, Kondareddiar; Tweedle, Michael F.; Linder, Karen; Nanjappan, Palaniappa; Raju, Natarajan
- PA USA
- SO U.S. Pat. Appl. Publ., 85 pp., Cont.-in-part of U.S. Ser. No. 585,364. CODEN: USXXCO
- DT Patent
- LA English
- IC ICM A61K038-16 ICS A61K051-08
- INCL 514008000
- CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 8, 34

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FAN.CNT 2
                             DATE
    PATENT NO.
                      KIND
                                       APPLICATION NO.
                                                             DATE
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                                      US 2001-871974
ΡI
    US 2002147136
                       A1
                             20021010
                                                             20010604
PRAI US 2000-585364
                       A2
                             20000602
CLASS
PATENT NO.
             CLASS PATENT FAMILY CLASSIFICATION CODES
US 2002147136 ICM
                     A61K038-16
               ICS
                     A61K051-08
               INCL
                     514008000
                     514/008.000; 514/021.000; 424/001.110
US 2002147136
               NCL
                     A61K047/48R2; A61K049/00P8; A61K049/22P8; A61K049/22P4;
               ECLA
                     A61K049/22P16; A61K051/08Z
    MARPAT 137:299916
    The present invention provides compds. for targeting endothelial cells,
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- OS
- AΒ tumor cells or other cells that express the neuropilin-1 (NP-1) receptor, compns. containing the same and methods for their use. The compds. are of the formula A-L-B (A = a monomer, multimer or polymer of TKPPR or analog which specifically binds to NP-1 or cells expressing NP-1 with avidity equal or greater than TKPPR; L = a lipid or a non-lipid (e.g., polymer) linker; B =a substrate). Addnl., the present invention includes diagnostic, therapeutic and radiotherapeutic compns. useful for visualization, therapy or radiotherapy. For example, DPPE-glutaroyl-Gly-Thr-Lys-Pro-Pro-Arg-OH (DPPE-Glu-GTKPPR) was prepared and formulated into gas-filled microbubble compns. for ultrasonic echog. The bubbles bind to human aortic endothelial cells (HAEC) under flow. The number of bubbles bound may increase with time for several minutes at a given flow rate, up to a flow rate producing 1.53 dynes/cm2, while bubbles without the targeting moiety (DPPE-Glu-GTKPPR) may not bind. However, once bound under a lesser flow rate (e.g., 1.53 dynes/cm2), the shear stress on bubbles containing DPPE-Glu-GTKPPR may be increased to 6.1 dynes/cm2 without dislodging many of the bound bubbles.
- ST peptide neuropilin receptor endothelium tumor targeting; antitumor angiogenesis inhibitor peptide deriv prepn; gene therapy radiotherapy peptide deriv; ultrasound imaging endothelium neuropilin peptide
- ΙT Fusion proteins (chimeric proteins)
 - RL: BSU (Biological study, unclassified); BIOL (Biological study) (KDR/Fc, binding to human aortic endothelial cells inhibition by; preparation of peptide-containing compds. and compns. for targeting cells expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
- TT Receptors
 - RL: BSU (Biological study, unclassified); BIOL (Biological study) (NP-1 (neuropilin-1); preparation of peptide-containing compds. and compns. for targeting cells expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
- IΤ Imaging agents
 - (acoustic imaging contrast agents; preparation of peptide-containing compds. and compns. for targeting cells expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
- тт Imaging
 - Imaging agents
 - (acoustic; preparation of peptide-containing compds. and compns. for targeting cells expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
- IT Artery
 - (aorta, endothelium, binding to; preparation of peptide-containing compds. and compns. for targeting cells expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
- IT Endothelium
 - (aortic, binding to; preparation of peptide-containing compds. and compns. for targeting cells expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
- IT Drug delivery systems
 - (beads; preparation of peptide-containing compds. and compns. for targeting

Audet 09/871974

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cells expressing neuropilin-1 receptor for diagnosis, imaging, and
TТ
     Diagnosis
     Diagnosis
        (cancer; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
IT
     Nucleic acids
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (delivery of; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
     Angiogenesis
IT
        (detection; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
        therapy)
IT
     Blood vessel
        (endothelium; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
IT
     Tumor necrosis factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (human aortic endothelial cells activated by; preparation of peptide-containing
        compds. and compns. for targeting cells expressing neuropilin-1
        receptor for diagnosis, imaging, and therapy)
     Drug delivery systems
IT
        (kits; preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
TT
     Drug delivery systems
        (liposomes; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
        therapy)
IT
     Fluorescent substances
        (markers; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
        therapy)
     Radionuclides, biological studies
IT
     RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
     USES (Uses)
        (markers; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
IΤ
     Air
        (microbubbles containing; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
ΤT
     Alkenes, biological studies
     Alkynes
     Hydrocarbons, biological studies
     Perfluorocarbons
     Perfluorocarbons
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (microbubbles containing; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
IT
     Drug delivery systems
        (microbubbles; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
TΤ
     Drug delivery systems
        (microparticles; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
IT
     Drug delivery systems
        (microspheres, fluorescent, peptide-conjugated; preparation of
        peptide-containing compds. and compns. for targeting cells expressing
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neuropilin-1 receptor for diagnosis, imaging, and therapy)
TΤ
     Peptides, preparation
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (oligopeptides; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
IT
        (particles; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
TT
     Angiogenesis inhibitors
     Drug delivery systems
     Drug screening
     Gene therapy
     Genetic vectors
     Human
     Imaging
     Imaging agents
     Radiopharmaceuticals
     Radiotherapy
     Reducing agents
     Sound and Ultrasound
     Viral vectors
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
IT
     Phospholipids, reactions
     Polymers, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
TТ
     Drug delivery systems
        (suspensions, gas-filled microbubbles containing; preparation of peptide-containing
        compds. and compns. for targeting cells expressing neuropilin-1
        receptor for diagnosis, imaging, and therapy)
TΤ
     Vascular endothelial growth factor receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (type VEGFR-2, activated, inhibition of; preparation of peptide-containing
        compds. and compns. for targeting cells expressing neuropilin-1
        receptor for diagnosis, imaging, and therapy)
IT
     Endothelium
        (vascular; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
IT
     9063-57-4, Tuftsin
                           127464-60-2, Vascular endothelial growth factor
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (binding to human aortic endothelial cells inhibition by; preparation of
        peptide-containing compds. and compns. for targeting cells expressing
        neuropilin-1 receptor for diagnosis, imaging, and therapy)
     14133-76-7DP, Technetium 99, complexes with tetrapeptide conjugate,
IT
     biological studies 470463-90-2DP, technetium 99 complexes
     RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses) (metastable; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
     124-38-9, Carbon dioxide, biological studies
                                                      2551-62-4, Sulfur
TT
                   7439-90-9, Krypton, biological studies 7440-37-1, Argon,
     hexafluoride
     biological studies 7440-63-3, Xenon, biological studies 7727-37-9, Nitrogen, biological studies 7782-44-7, Oxygen, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (microbubbles containing; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
     imaging, and therapy)
214210-47-6, Neuropilin-1
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
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(preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
ΙT
     377087-52-0P, BRU 305
     RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic
     preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant
     or reagent)
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
IT
     377087-53-1P, BRU 306
     RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);
     BIOL (Biological study); PREP (Preparation)
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
TТ
     377087-63-3P, BRU 317 377087-82-6P, BRU 239
     377088-92-1P, BRU 337 377088-93-2P, BRU 346
     377725-24-1P, BRU 326 468726-69-4P 468729-71-7P
     470463-86-6P, BRU 292 470463-90-2P, BRU 363
     RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
                                                  1663-39-4, tert-Butyl
IT
     100-46-9, Benzylamine, reactions 1155-64-2
               4530-20-5, Boc-glycine 5681-36-7,
     Dipalmitoylphosphatidylethanolamine 7672-27-7
                                                      15401-08-8
                                                                    29022-11-5,
     Fmoc-glycine 33662-26-9 71989-26-9 71989-35-0 82911-69-1
     106392-12-5, Poloxamer F 108 120791-76-6 129223-22-9 166108-71-0
     167393-62-6 169543-81-1 198139-51-4 251450-64-3 283176-26-1
     377087-81-5D, resin bound 377087-83-7D, resin-bound
     470444-40-7, BRU 351
     RL: RCT (Reactant); RACT (Reactant or reagent) (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
     4246-51-9P, 4,7,10-Trioxa-1,13-tridecanediamine 128988-04-5P
     150525-42-1P 377087-49-5P 377087-50-8P 377087-57-5P
     377087-58-6P
                   377087-59-7P 377087-60-0P 377087-62-2P
     377087-64-4P
                   377087-65-5P
                                  377087-66-6P
                                                 377087-67-7P
                                                                 377087-69-9P
                  377087-71-3P
                                 377087-72-4P
                                                 377087-73-5P
                                                                 377087-74-6P
     377087-70-2P
     377087-76-8P 377087-77-9P 377087-78-0P 377087-79-1P
     377087-80-4P 377088-94-3P
                                  468726-65-0P
                                                  468726-66-1P
     468726-68-3P 468726-70-7P 468726-71-8P
                                                 468726-77-4DP,
     468726-73-0P
                  468726-75-2DP, resin bound
                  468729-73-9P 468729-75-1P
     resin-bound
                                                468729-78-4P
                                                              470463-87-7P
     470463-88-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
IT
     41961-58-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
     USES (Uses)
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
     10098-91-6, Yttrium 90, biological studies 13967-64-1, Dysprosium 165,
IT
     biological studies 13967-65-2, Holmium 166, biological studies
     13968-53-1, Ruthenium 103, biological studies
                                                    13981-25-4, Copper 64,
    biological studies 13982-36-0, Yttrium 88, biological studies
                                                14265-75-9, Lutetium 177,
     14119-09-6, Gallium 67, biological studies
     biological studies 14378-26-8, Rhenium 188, biological studies
     14913-89-4, biological studies 14998-63-1, Rhenium 186, biological
             15750-15-9, Indium 111, biological studies
                                                          15757-14-9, Gallium
     68, biological studies 15758-35-7, Ruthenium 97, biological studies
     15766-00-4, Samarium 153, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (preparation of radiolabeled peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
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imaging, and therapy)
     42074-68-0 468726-76-3
IT
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (resin-bound; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
IT
     470463-90-2DP, technetium 99 complexes
     RL: RCT (Reactant); RACT (Reactant or reagent); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
        (metastable; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
        therapy)
     470463-90-2 HCAPLUS
RN
     L-Arginine, N-[10,18-bis(hydroxyimino)-11,11,17,17-tetramethyl-1,6-dioxo-
CN
     15-oxa-7,12,16-triazanonadec-1-yl]glycyl-N-(2-carboxyethyl)-β-
     alanylglycyl-N-[3-[[2-[2-(carboxymethoxy)ethoxy]ethyl]amino]-3-oxopropyl]-
     β-alanyl [2-(2-aminoethoxy) ethoxy] acetyl-L-threonyl-L-lysyl-L-prolyl-L-
     prolyl-, (2\rightarrow1')-amide with glycyl-N-[3-[[2-[2-
     (carboxymethoxy)ethoxy]ethyl]amino]-3-oxopropyl]-β-alanyl[2-(2-
     aminoethoxy) ethoxy] acetyl-L-threonyl-L-lysyl-L-prolyl-L-prolyl-L-arginine
     (2'→1'')-amide with L-threonyl-L-lysyl-L-prolyl-L-
     arginine, (4→1''')-amide with L-threonyl-L-lysyl-L-prolyl-L-prolyl-
     L-arginine (9CI) (CA INDEX NAME)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
     ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN .
L7
AΝ
     2001:885834 HCAPLUS
DN
     136:25104
ED
     Entered STN: 07 Dec 2001
     Peptide-containing compounds for targeting endothelial cells, compositions
TI
     containing the same and methods for their use
IN
     Von Wronski, Mathew A.; Marinelli, Edmund R.; Nunn, Adrian D.; Pillai,
     Radhakrishna; Ramalingam, Kondareddiar; Tweedle, Michael F.; Linder,
     Karen; Nanjappan, Palaniappa; Raju, Natarajan
     Bracco Research USA, USA
PA
SO
     PCT Int. Appl., 146 pp.
     CODEN: PIXXD2
DT
     Patent
LА
     English
     ICM A61K051-00
IC
     63-6 (Pharmaceuticals)
CC
     Section cross-reference(s): 1, 8, 9, 34, 35
FAN.CNT 2
                                             APPLICATION NO.
     PATENT NO.
                         KIND
                                DATE
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PΙ
     WO 2001091805
                          A2
                                 20011206
                                             WO 2001-US18053
                                                                     20010604
                                 20020906
     WO 2001091805
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         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2410887
                          AA
                                 20011206
                                            CA 2001-2410887
                                 20030312
                                            EP 2001-944270
     EP 1289565
                          A2
                                                                     20010604
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             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                                             JP 2001-587817
     JP 2004500854
                          T2
                                 20040115
                                                                     20010604
PRAI US 2000-585364
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     WO 2001-US18053
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CLASS

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PATENT NO.
                  CLASS PATENT FAMILY CLASSIFICATION CODES
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 WO 2001091805
                  ICM
                         A61K051-00
                         A61K047/48R2; A61K049/00P8; A61K049/22P4; A61K049/22P8;
 WO 2001091805
                  ECLA
                         A61K049/22P16; A61K051/08Z
                        4B024/AA01; 4B024/AA20; 4B024/CA02; 4B024/DA02;
 JP 2004500854
                  FTERM
                         4B024/DA03; 4B024/GA11; 4B024/HA17; 4B063/QA05;
                         4B063/QQ21; 4B063/QQ41; 4B063/QQ61; 4B063/QQ89;
                         4B063/QQ91; 4B063/QR51; 4B063/QR59; 4B063/QR77;
                         4B063/QS31; 4B063/QS36; 4B063/QS39; 4B063/QX01;
                         4B063/QX10; 4B065/AA90X; 4B065/AA93X; 4B065/AB01;
                         4B065/AB10; 4B065/AC14; 4B065/BA02; 4B065/BA30; 4B065/CA24; 4B065/CA43; 4B065/CA44; 4B065/CA46;
                         4C076/CC27; 4C076/DD41; 4C076/DD44; 4C076/DD45;
                         4C076/DD46; 4C076/DD51; 4C076/DD52; 4C076/DD59;
                         4C076/DD63; 4C076/DD68; 4C076/DD69; 4C076/DD70;
                         4C076/EE06; 4C076/EE30; 4C076/EE59; 4C084/AA02;
                         4C084/AA12; 4C084/BA17; 4C084/BA18; 4C084/BA42; 4C084/DA03; 4C084/NA14; 4C084/ZB26; 4H045/AA10;
                         4H045/AA20; 4H045/BA13; 4H045/BA50; 4H045/BA55;
                         4H045/EA20; 4H045/EA50; 4H045/FA31; 4H045/FA41;
                         4H045/FA50; 4H045/FA58
os
     MARPAT 136:25104
     The present invention provides compds. for targeting endothelial cells,
AB
     tumor cells or other cells that express the neuropilin-1 (NP-1) receptor,
     compns. containing the same and methods for their use. The compds. are of the
     formula A-L-B (A = TKPPR or analog which specifically binds to an
     endothelial cell or cells that express markers in common with endothelial
     cells, with equal or greater avidity as TKPPR; L = a lipid or a non-lipid
     (polymer) linker; B = a substrate). Addnl., the present invention includes diagnostic, therapeutic and radiotherapeutic compns. useful for
     visualization, therapy or radiotherapy. For example, DPPE-glutaroyl-Gly-
     Thr-Lys-Pro-Pro-Arg-OH (DPPE-Glu-GTKPPR) was prepared and formulated into
     gas-filled microbubble compns. for ultrasonic echog. The bubbles interact
     with a VEGF receptor on human aortic endothelial cells (HAEC), possibly
     with KDR receptor, or more likely with NP-1 receptor which binds to KDR.
ST
     peptide neuropilin receptor endothelium targeting diagnosis therapy;
     antitumor angiogenesis inhibitor peptide deriv prepn; gene therapy
     radiotherapy peptide deriv; ultrasound imaging endothelium neuropilin
     peptide
IT
     Imaging agents
        (acoustic imaging contrast agents; preparation of peptide-containing compds. and
        compns. for targeting endothelial cells expressing neuropilin-1
        receptor for diagnosis and therapy)
TT
     Imaging
        (acoustic; preparation of peptide-containing compds. and compns. for targeting
        endothelial cells expressing neuropilin-1 receptor for diagnosis and
        therapy)
IT
     Arterv
        (aorta, endothelium; preparation of peptide-containing compds. and compns. for
        targeting endothelial cells expressing neuropilin-1 receptor for
        diagnosis and therapy)
IT
     Endothelium
        (aortic; preparation of peptide-containing compds. and compns. for targeting
        endothelial cells expressing neuropilin-1 receptor for diagnosis and
        therapy)
IT
     Drug delivery systems
        (beads; preparation of peptide-containing compds. and compns. for targeting
        endothelial cells expressing neuropilin-1 receptor for diagnosis and
        therapy)
IT
     Diagnosis
     Diagnosis
        (cancer; preparation of peptide-containing compds. and compns. for targeting
        endothelial cells expressing neuropilin-1 receptor for diagnosis and
        therapy)
IT
     Antitumor agents
```

```
(carcinoma, epidermoid; preparation of peptide-containing compds. and compns.
        for targeting endothelial cells expressing neuropilin-1 receptor for
        diagnosis and therapy)
ΙT
     Polyoxyalkylenes, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (derivs.; preparation of peptide-containing compds. and compns. for targeting
        endothelial cells expressing neuropilin-1 receptor for diagnosis and
        therapy)
    Angiogenesis
IT
        (detection; preparation of peptide-containing compds. and compns. for targeting
        endothelial cells expressing neuropilin-1 receptor for diagnosis and
        therapy)
IT
    Diglycerides
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (digalactosyl; preparation of peptide-containing compds. and compns. for
        targeting endothelial cells expressing neuropilin-1 receptor for
        diagnosis and therapy)
ΙT
    Cell activation
        (endothelial; preparation of peptide-containing compds. and compns. for
        targeting endothelial cells expressing neuropilin-1 receptor for
        diagnosis and therapy)
IT
     Blood vessel
     Blood vessel
        (endothelium; preparation of peptide-containing compds. and compns. for
        targeting endothelial cells expressing neuropilin-1 receptor for
        diagnosis and therapy)
     Fatty acids, biological studies
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (esters, with lipids; preparation of peptide-containing compds. and compns. for
        targeting endothelial cells expressing neuropilin-1 receptor for
        diagnosis and therapy)
IT
    Sterols
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (esters, with sugar acids; preparation of peptide-containing compds. and compns.
        for targeting endothelial cells expressing neuropilin-1 receptor for
        diagnosis and therapy)
    Lipids, biological studies
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (ether-linked, with fatty acids; preparation of peptide-containing compds. and
        compns. for targeting endothelial cells expressing neuropilin-1
        receptor for diagnosis and therapy)
IT
     Vascular endothelial growth factor receptors
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (interaction with; preparation of peptide-containing compds. and compns. for
        targeting endothelial cells expressing neuropilin-1 receptor for
        diagnosis and therapy)
IT
    Drug delivery systems
        (liposomes; preparation of peptide-containing compds. and compns. for targeting
        endothelial cells expressing neuropilin-1 receptor for diagnosis and
        therapy)
    Alcohols, biological studies
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (long-chain; preparation of peptide-containing compds. and compns. for targeting
        endothelial cells expressing neuropilin-1 receptor for diagnosis and
        therapy)
TΤ
     Fluorescent substances
        (markers; preparation of peptide-containing compds. and compns. for targeting
        endothelial cells expressing neuropilin-1 receptor for diagnosis and
        therapy)
    Radionuclides, biological studies
TΥ
     RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
     USES (Uses)
        (markers; preparation of peptide-containing compds. and compns. for targeting
        endothelial cells expressing neuropilin-1 receptor for diagnosis and
        therapy)
    Drug delivery systems
IT
```

```
(microbubbles, gas-filled; preparation of peptide-containing compds. and compns.
        for targeting endothelial cells expressing neuropilin-1 receptor for
        diagnosis and therapy)
IT
     Drug delivery systems
        (microspheres; preparation of peptide-containing compds. and compns. for
        targeting endothelial cells expressing neuropilin-1 receptor for
        diagnosis and therapy)
IT
     Liposomes
     Surfactants
        (nonionic; preparation of peptide-containing compds. and compns. for targeting
        endothelial cells expressing neuropilin-1 receptor for diagnosis and
        therapy)
     Peptides, biological studies
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (oligopeptides; preparation of peptide-containing compds. and compns. for
        targeting endothelial cells expressing neuropilin-1 receptor for
        diagnosis and therapy)
ΙT
     Phosphoproteins
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (phosphotyrosine-containing, phosphorylation; preparation of peptide-containing
        compds. and compns. for targeting endothelial cells expressing
        neuropilin-1 receptor for diagnosis and therapy)
IT
     Air
     Angiogenesis inhibitors
     Animal
     Antitumor agents
     Diagnosis
     Drug delivery systems
     Drug delivery systems
     Gene therapy
     Genetic vectors
     Human
     Imaging
     Imaging agents
     Radiopharmaceuticals
     Radiotherapy
     Reducing agents
     Retroviral vectors
     Sound and Ultrasound
     Viral vectors
        (preparation of peptide-containing compds. and compns. for targeting endothelial
        cells expressing neuropilin-1 receptor for diagnosis and therapy)
     Alkenes, biological studies
TΤ
     Alkynes
     Cardiolipins
     Ceramides
     Fatty acids, biological studies
     Glycolipids
     Glycosphingolipids
     Hydrocarbons, biological studies
     Lipids, biological studies
     Lipopolysaccharides
     Lysophospholipids
     Nucleic acids
     Perfluorocarbons
     Perfluorocarbons
     Phosphatidic acids
     Phosphatidylinositols
     Phospholipids, biological studies
     Polymers, biological studies
     Saponins
     Sphingolipids
     Sulfatides
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (preparation of peptide-containing compds. and compns. for targeting endothelial
        cells expressing neuropilin-1 receptor for diagnosis and therapy)
```

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Phosphorylation, biological
        (protein, protein tyrosines; preparation of peptide-containing compds. and
        compns. for targeting endothelial cells expressing neuropilin-1
        receptor for diagnosis and therapy)
IT
     Carbohydrates, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (sugar esters, with aliphatic acids; preparation of peptide-containing compds. and
        compns. for targeting endothelial cells expressing neuropilin-1
        receptor for diagnosis and therapy)
ΙT
     Drug delivery systems
        (suspensions; preparation of peptide-containing compds. and compns. for
        targeting endothelial cells expressing neuropilin-1 receptor for
        diagnosis and therapy)
     Vascular endothelial growth factor receptors
ΙT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (type VEGFR-2, interaction with; preparation of peptide-containing compds. and
        compns. for targeting endothelial cells expressing neuropilin-1
        receptor for diagnosis and therapy)
ΙT
     Endothelium
     Endothelium
        (vascular; preparation of peptide-containing compds. and compns. for targeting
        endothelial cells expressing neuropilin-1 receptor for diagnosis and
        therapy)
     127464-60-2, Vascular endothelial growth factor
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (binding to neuropilin-1 and KDR receptors; preparation of peptide-containing
        compds. and compns. for targeting endothelial cells expressing
        neuropilin-1 receptor for diagnosis and therapy)
     14133-76-7DP, Technetium 99, complexes with tetrapeptide conjugate,
IT
     biological studies
     RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (metastable; preparation of peptide-containing compds. and compns. for targeting
        endothelial cells expressing neuropilin-1 receptor for diagnosis and
        therapy)
     56-12-2, \gamma-Aminobutyric acid, biological studies
                                                        56-40-6, Glycine,
     biological studies 56-84-8, L-Aspartic acid, biological studies
     56-86-0, L-Glutamic acid, biological studies
                                                    1197-18-8,
     trans-4-Aminomethylcyclohexanecarboxylic acid
                                                     9063-57-4, Tuftsin
     214210-47-6, Neuropilin-1
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (preparation of peptide-containing compds. and compns. for targeting endothelial
        cells expressing neuropilin-1 receptor for diagnosis and therapy)
     41961-58-4DP, conjugates with red fluorescent carboxylate-modified
IT
                 145018-54-8DP, FluoSphere, red fluorescent
     carboxylate-modified, conjugates with peptide
     RL: BSU (Biological study, unclassified); DGN (Diagnostic use); SPN
     (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
     PREP (Preparation); USES (Uses)
        (preparation of peptide-containing compds. and compns. for targeting endothelial
        cells expressing neuropilin-1 receptor for diagnosis and therapy)
TТ
     41961-58-4P
     RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic
     preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant
     or reagent)
        (preparation of peptide-containing compds. and compns. for targeting endothelial
        cells expressing neuropilin-1 receptor for diagnosis and therapy)
     377087-37-1P 377087-53-1P 377087-54-2P
IT
     377087-63-3P 377087-82-6P 377088-92-1P
     377088-93-2P 377725-24-1P 377725-30-9P
    RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of peptide-containing compds. and compns. for targeting endothelial
        cells expressing neuropilin-1 receptor for diagnosis and therapy)
                                  72-19-5, L-Threonine, reactions
                                                                      108-55-4,
IΤ
     56-87-1, L-Lysine, reactions
     Glutaric anhydride 1155-64-2 1663-39-4, tert-Butyl acrylate
```

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15260-10-3 15401-08-8 15401-08-8
                            7672-27-7
     2149-70-4 4530-20-5
               71989-26-9 71989-35-0 129223-22-9 135821-02-2
     29022-11-5
                 167393-62-6
                                169543-81-1
                                             195136-58-4
     166108-71-0
                                                           377087-58-6
                  377087-81-5
                                377087-84-8
     377087-61-1
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of peptide-containing compds. and compns. for targeting endothelial
        cells expressing neuropilin-1 receptor for diagnosis and therapy)
IT
    128988-04-5P
                  198139-51-4P 377087-43-9P
                                                377087-44-0P
     377087-45-1P
                   377087-46-2P
                                 377087-47-3P 377087-48-4P
     377087-49-5P 377087-50-8P 377087-51-9P
     377087-52-0P 377087-55-3P 377087-56-4P
     377087-57-5P
                   377087-59-7P 377087-60-0P 377087-62-2P
                 377087-65-5P
                                 377087-66-6P 377087-67-7P
                                                               377087-68-8P
    377087-64-4P
     377087-69-9P 377087-70-2P
                                  377087-71-3P
                                                 377087-72-4P
                                                               377087-73-5P
     377087-74-6P 377087-75-7P 377087-76-8P
                                               377087-77-9P
     377087-78-0P 377087-79-1P 377087-80-4P
     377088-94-3P 377725-26-3P 377725-28-5P
                                                 377725-29-6P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of peptide-containing compds. and compns. for targeting endothelial
       cells expressing neuropilin-1 receptor for diagnosis and therapy)
    2462-63-7 5681-36-7, Dipalmitoylphosphatidylethanolamine
TT
     106392-12-5, Ethylene oxide-propylene oxide block copolymer
    RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological
    study); RACT (Reactant or reagent); USES (Uses)
        (preparation of peptide-containing compds. and compns. for targeting endothelial
       cells expressing neuropilin-1 receptor for diagnosis and therapy)
IT
     56-81-5, Glycerol, biological studies 56-81-5D, Glycerol, esters
     57-88-5, Cholesterol, biological studies 110-15-6, Succinic acid,
    biological studies 110-94-1, Glutaric acid 124-30-1, Stearylamine
    124-38-9, Carbon dioxide, biological studies
                                                  141-82-2, Malonic acid,
    biological studies 144-62-7, Oxalic acid, biological studies
                         1256-86-6, Cholesterol sulfate 1510-21-0,
    Glycerol trilaurate
    Cholesterol hemisuccinate 2197-63-9, Dicetyl phosphate
                                                              2551-62-4,
    Sulfur hexafluoride 3614-36-6, Diacetyl phosphate 4345-03-3
    4537-76-2, Distearoylphosphatidylethanolamine 7439-90-9, Krypton,
    biological studies 7440-37-1, Argon, biological studies
    Xenon, biological studies 7727-37-9, Nitrogen, biological studies
    7782-44-7, Oxygen, biological studies 9002-89-5, Polyvinyl alcohol
    9004-54-0D, Dextran, derivs.
                                  10098-91-6, Yttrium-90, biological studies
    13967-64-1, Dysprosium-165, biological studies 13967-65-2, Holmium-166,
    biological studies 13968-53-1, Ruthenium-103, biological studies
    13981-25-4, Copper-64, biological studies 13982-36-0, Yttrium-88,
    biological studies 14119-09-6, Gallium-67, biological studies
    14133-76-7, Technetium-99, biological studies 14265-75-9, Lutetium-177,
    biological studies 14378-26-8, Rhenium-188, biological studies
    14913-89-4, biological studies 14998-63-1, Rhenium-186, biological
             15750-15-9, Indium-111, biological studies 15757-14-9,
    studies
    Gallium-68, biological studies 15758-35-7, Ruthenium-97, biological
    studies 15766-00-4, Samarium-153, biological studies 20255-95-2,
    Dimyristoylphosphatidylethanolamine
                                         24529-88-2
                                                      25322-68-3D,
    Polyethylene glycol, derivs. 26657-95-4, Glycerol dipalmitate
    27638-00-2, Glycerol dilaurate 55252-82-9
                                                68354-92-7
                                                              73294-85-6
                 78543-25-6, 1-Hexadecyl-2-palmitoylglycerophosphoethanolamine
    76822-97-4
                              108032-13-9
                                           161293-59-0
    83554-62-5
                 87136-19-4
                                                         161441-83-4
                 377088-91-0
    186198-32-3
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (preparation of peptide-containing compds. and compns. for targeting endothelial
       cells expressing neuropilin-1 receptor for diagnosis and therapy)
IT
    4246-51-9, 4,7,10-Trioxa-1,13-tridecanediamine 377087-83-7
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (support-bound; preparation of peptide-containing compds. and compns. for
       targeting endothelial cells expressing neuropilin-1 receptor for
       diagnosis and therapy)
    41961-58-4DP, conjugates with red fluorescent carboxylate-modified
IT
    FluoSphere
```

RL: RCT (Reactant); DGN (Diagnostic use); SPN (Synthetic preparation); RACT (Reactant or reagent); BIOL (Biological

study); PREP (Preparation); USES (Uses)

(preparation of peptide-containing compds. and compns. for targeting endothelial cells expressing neuropilin-1 receptor for diagnosis and therapy)

RN

41961-58-4 HCAPLUS L-Arginine, L-threonyl-L-lysyl-L-prolyl-L-prolyl- (9CI) (CA INDEX NAME) CN

Absolute stereochemistry.

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FILE 'HCAPLUS' ENTERED AT 15:08:41 ON 08 JUL 2005 L2 TRA L1 1- RN : 103 TERMS

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- L1 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
- AN 2002:778699 HCAPLUS
- DN 137:299916
- ED Entered STN: 11 Oct 2002
- TI Peptide-containing compounds for targeting cells expressing NP-1 receptor
- IN Von Wronski, Mathew A.; Marinelli, Edmund R.; Nunn, Adrian D.; Pillai, Radhakrishna; Ramalingam, Kondareddiar; Tweedle, Michael F.; Linder, Karen; Nanjappan, Palaniappa; Raju, Natarajan
- PA US.
- SO U.S. Pat. Appl. Publ., 85 pp., Cont.-in-part of U.S. Ser. No. 585,364. CODEN: USXXCO
- DT Patent
- LA English
- IC ICM A61K038-16 ICS A61K051-08
- INCL 514008000
- CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 8, 34

FAN.CNT 2

PATENT NO. KIND DATE APPLICATION NO. DATE

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                                           US 2001-871974
   US 2002147136
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                               20021010
PRAI US 2000-585364
                               20000602
                         A2
CLASS
               CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
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                       A61K038-16
                ICM
 US 2002147136
                ICS
                       A61K051-08
                INCL 514008000
 US 2002147136
               NCL
                       514/008.000; 514/021.000; 424/001.110
                       A61K047/48R2; A61K049/00P8; A61K049/22P8; A61K049/22P4;
                ECLA
                       A61K049/22P16; A61K051/08Z
OS
    MARPAT 137:299916
    The present invention provides compds. for targeting endothelial cells,
AB
     tumor cells or other cells that express the neuropilin-1 (NP-1) receptor,
    compns. containing the same and methods for their use. The compds. are of the
     formula A-L-B (A = a monomer, multimer or polymer of TKPPR or analog which
     specifically binds to NP-1 or cells expressing NP-1 with avidity equal or
     greater than TKPPR; L = a lipid or a non-lipid (e.g., polymer) linker; B =
     a substrate). Addnl., the present invention includes diagnostic,
     therapeutic and radiotherapeutic compns. useful for visualization, therapy
     or radiotherapy. For example, DPPE-glutaroyl-Gly-Thr-Lys-Pro-Pro-Arg-OH
     (DPPE-Glu-GTKPPR) was prepared and formulated into gas-filled microbubble
     compns. for ultrasonic echog. The bubbles bind to human aortic
     endothelial cells (HAEC) under flow. The number of bubbles bound may
     increase with time for several minutes at a given flow rate, up to a flow
     rate producing 1.53 dynes/cm2, while bubbles without the targeting moiety
     (DPPE-Glu-GTKPPR) may not bind. However, once bound under a lesser flow
     rate (e.g., 1.53 dynes/cm2), the shear stress on bubbles containing
     DPPE-Glu-GTKPPR may be increased to 6.1 dynes/cm2 without dislodging many
     of the bound bubbles.
    peptide neuropilin receptor endothelium tumor targeting; antitumor
ST
     angiogenesis inhibitor peptide deriv prepn; gene therapy radiotherapy
     peptide deriv; ultrasound imaging endothelium neuropilin peptide
ΙT
     Fusion proteins (chimeric proteins)
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (KDR/Fc, binding to human aortic endothelial cells inhibition by;
       preparation of peptide-containing compds. and compns. for targeting cells
       expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
TΤ
    Receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (NP-1 (neuropilin-1); preparation of peptide-containing compds. and compns. for
       targeting cells expressing neuropilin-1 receptor for diagnosis,
       imaging, and therapy)
IT
     Imaging agents
        (acoustic imaging contrast agents; preparation of peptide-containing compds. and
        compns. for targeting cells expressing neuropilin-1 receptor for
       diagnosis, imaging, and therapy)
IT
    Imaging
        (acoustic; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
        therapy)
IT
        (aorta, endothelium, binding to; preparation of peptide-containing compds. and
        compns. for targeting cells expressing neuropilin-1 receptor for
        diagnosis, imaging, and therapy)
IT
     Endothelium
        (aortic, binding to; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
    Drug delivery systems
IT
        (beads; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
       therapy)
IT
    Diagnosis
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Diagnosis

```
(cancer; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
        therapy)
TТ
     Nucleic acids
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (delivery of; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
     Angiogenesis
IT
        (detection; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
        therapy)
IT
     Blood vessel
        (endothelium; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
TT
     Tumor necrosis factors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (human aortic endothelial cells activated by; preparation of peptide-containing
        compds. and compns. for targeting cells expressing neuropilin-1
        receptor for diagnosis, imaging, and therapy)
IT
     Drug delivery systems
        (kits; preparation of peptide-containing compds. and compns. for targeting cells expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
IT
     Drug delivery systems
        (liposomes; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
        therapy)
IT
     Fluorescent substances
        (markers; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
        therapy)
IT
     Radionuclides, biological studies
     RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);
     USES (Uses)
        (markers; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
        therapy)
тт
     Air
        (microbubbles containing; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
IT Alkenes, biological studies
     Alkynes
     Hydrocarbons, biological studies
     Perfluorocarbons
     Perfluorocarbons
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (microbubbles containing; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
TТ
     Drug delivery systems
        (microbubbles; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
TТ
     Drug delivery systems
        (microparticles; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
TT
     Drug delivery systems
        (microspheres, fluorescent, peptide-conjugated; preparation of
        peptide-containing compds. and compns. for targeting cells expressing
        neuropilin-1 receptor for diagnosis, imaging, and therapy)
IT
     Peptides, preparation
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
```

```
(oligopeptides; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
IT
     Virus
        (particles; preparation of peptide-containing compds. and compns. for targeting cells expressing neuropilin-1 receptor for diagnosis, imaging, and
IT
     Angiogenesis inhibitors
     Drug delivery systems
     Drug screening
     Gene therapy
     Genetic vectors
     Human
     Imaging
     Imaging agents
     Radiopharmaceuticals
     Radiotherapy
     Reducing agents
     Sound and Ultrasound
     Viral vectors
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
TT
     Phospholipids, reactions
     Polymers, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
IT
     Drug delivery systems
        (suspensions, gas-filled microbubbles containing; preparation of peptide-containing
        compds. and compns. for targeting cells expressing neuropilin-1
        receptor for diagnosis, imaging, and therapy)
IT
     Vascular endothelial growth factor receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (type VEGFR-2, activated, inhibition of; preparation of peptide-containing
        compds. and compns. for targeting cells expressing neuropilin-1
        receptor for diagnosis, imaging, and therapy)
IT
     Endothelium
        (vascular; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
        therapy)
                          127464-60-2, Vascular endothelial growth factor
IT
     9063-57-4, Tuftsin
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (binding to human aortic endothelial cells inhibition by; preparation of
        peptide-containing compds. and compns. for targeting cells expressing
        neuropilin-1 receptor for diagnosis, imaging, and therapy)
IT
     14133-76-7DP, Technetium 99, complexes with tetrapeptide conjugate,
     biological studies 470463-90-2DP, technetium 99 complexes
     RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic
     use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (metastable; preparation of peptide-containing compds. and compns. for targeting
        cells expressing neuropilin-1 receptor for diagnosis, imaging, and
        therapy)
IT
     124-38-9, Carbon dioxide, biological studies 2551-62-4, Sulfur
                    7439-90-9, Krypton, biological studies 7440-37-1, Argon,
     hexafluoride
     biological studies
                         7440-63-3, Xenon, biological studies
                                                                 7727-37-9,
     Nitrogen, biological studies 7782-44-7, Oxygen, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (microbubbles containing; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
ΤT
    214210-47-6, Neuropilin-1
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
ΙT
     377087-52-0P, BRU 305
     RL: BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic
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preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant
    or reagent)
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
IT
    377087-53-1P, BRU 306
     RL: BSU (Biological study, unclassified); SPN (Synthetic preparation);
    BIOL (Biological study); PREP (Preparation)
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
                                                   377088-92-1P, BRU 337
TT
    377087-63-3P, BRU 317
                           377087-82-6P, BRU 239
     377088-93-2P, BRU 346
                            377725-24-1P, BRU 326
                                                    468726-69-4P
     468729-71-7P 470463-86-6P, BRU 292
                                           470463-90-2P, BRU 363
    RL: DGN (Diagnostic use); SPN (Synthetic preparation); THU (Therapeutic
    use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
    100-46-9, Benzylamine, reactions 1155-64-2 1663-39-4, tert-Butyl
IT
               4530-20-5, Boc-glycine
                                        5681-36-7,
     acrylate
    Dipalmitoylphosphatidylethanolamine 7672-27-7
                                                      15401-08-8
                                                                    29022-11-5.
    Fmoc-glycine
                   33662-26-9 71989-26-9 71989-35-0
                                                         82911-69-1
    106392-12-5, Poloxamer F 108
                                   120791-76-6
                                                129223-22-9
                                                               166108-71-0
                  169543-81-1 198139-51-4 251450-64-3 283176-26-1
    167393-62-6
    377087-81-5D, resin bound
                               377087-83-7D, resin-bound 470444-40-7, BRU
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
    4246-51-9P, 4,7,10-Trioxa-1,13-tridecanediamine 128988-04-5P
IT
                                  377087-50-8P
     150525-42-1P
                   377087-49-5P
                                                 377087-57-5P
                                                                 377087-58-6P
                                  377087-62-2P
    377087-59-7P
                   377087-60-0P
                                                 377087-64-4P
                                                                 377087-65-5P
    377087-66-6P
                  377087-67-7P
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                                                 377087-70-2P
                                                                 377087-71-3P
    377087-72-4P
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                  377087-73-5P 377087-74-6P
                                                                 377087-77-9P
                                                 377088-94-3P
    377087-78-0P
                  377087-79-1P
                                 377087-80-4P
                                                                 468726-65-0P
                   468726-68-3P
                                  468726-70-7P
                                                 468726-71-8P
                                                                 468726-73-0P
    468726-66-1P
    468726-75-2DP, resin bound 468726-77-4DP, resin-bound 468729-73-9P 468729-75-1P 468729-78-4P 470463-87-7P 470463-88-8P
    RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of peptide-containing compds. and compns. for targeting cells
        expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
IT
     41961-58-4P
    RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);
    BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
        (preparation of peptide-containing compds. and compns. for targeting cells
       expressing neuropilin-1 receptor for diagnosis, imaging, and therapy)
    10098-91-6, Yttrium 90, biological studies 13967-64-1, Dysprosium 165,
TТ
    biological studies 13967-65-2, Holmium 166, biological studies
    13968-53-1, Ruthenium 103, biological studies
                                                   13981-25-4, Copper 64,
    biological studies 13982-36-0, Yttrium 88, biological studies
     14119-09-6, Gallium 67, biological studies
                                                14265-75-9, Lutetium 177,
    biological studies 14378-26-8, Rhenium 188, biological studies
     14913-89-4, biological studies 14998-63-1, Rhenium 186, biological
              15750-15-9, Indium 111, biological studies 15757-14-9, Gallium
                            15758-35-7, Ruthenium 97, biological studies
     68, biological studies
     15766-00-4, Samarium 153, biological studies
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (preparation of radiolabeled peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
        imaging, and therapy)
IT
     42074-68-0
                 468726-76-3
    RL: RCT (Reactant); RACT (Reactant or reagent)
        (resin-bound; preparation of peptide-containing compds. and compns. for
        targeting cells expressing neuropilin-1 receptor for diagnosis,
       imaging, and therapy)
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     ANSWER 1 OF 1 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
L4
AN
     2003-800817 [75]
CR
     2002-195523 [25]
DNC C2003-221021
     Composition used in targeting endothelial cells e.g. tumor cells comprises
     compounds containing monomers, multimers or polymers of
     L-arginine-L-threonyl-L-lysyl-L-prolyl-L-prolyl.
DC
     A96 B04 K08
TN
     LINDER, K; MARINELLI, E R; NANJAPPAN, P; NUNN, A D; PILLAI, R; RAJU, N;
     RAMALINGAM, K; TWEEDLE, M F; VON WRONSKI, M A
     (LIND-I) LINDER K; (MARI-I) MARINELLI E R; (NANJ-I) NANJAPPAN P; (NUNN-I)
PΑ
     NUNN A D; (PILL-I) PILLAI R; (RAJU-I) RAJU N; (RAMA-I) RAMALINGAM K;
     (TWEE-I) TWEEDLE M F; (VWRO-I) VON WRONSKI M A
CYC
PΤ
     US 2002147136 A1 20021010 (200375)*
                                                85
                                                      A61K038-16
ADT US 2002147136 A1 CIP of US 2000-585364 20000602, US 2001-871974 20010604
PRAI US 2001-871974
                          20010604; US 2000-585364
                                                         20000602
IC
     ICM A61K038-16
     ICS
         A61K051-08
AB
     US2002147136 A UPAB: 20031120
     NOVELTY - Composition (A1) comprises compounds containing monomers,
     multimers or polymers of L-arginine-L-threonyl-L-lysyl-L-prolyl-L-prolyl.
          DETAILED DESCRIPTION - Composition (A1) comprises a compound
     containing monomers, multimers or polymers of L-arginine-L-threonyl-L-
     lysyl-L-prolyl-L-prolyl (TKPPR) of formula A-L-B1 (I).
          A = monomer, multimer or polymer of TKPPR or its analogue that
     specifically binds to NP-1 or cells that express NP-1 with avidity of at
     least that of TKPPR;
          L = a linker (preferably a group of formula (i));
          X = NH, NR, O, S or SR;
     m = 0-2;
     n = 0-4;
          R = H or 1-4C alkyl (optionally substituted by at least one OH), and
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B1 = a substrate.
          INDEPENDENT CLAIMS are also included for:
          (1) a compound of formula A-L-Bla (II) and A-L-B3 (III) for use in
     targeting endothelial cells, tumor cells or other cells;
          (2) an ultrasound contrast agent (c1) comprising a suspension of gas
     filled microbubbles comprising (II);
          (3) an ultrasound contrast agent (c2) comprising a suspension of gas
     filled microballoons comprising (III);
          (4) preparation of (I) which comprises conjugating the monomer,
     multimer or polymer of TKPRR or its analogue with a linker to obtain a
     compound of formula A-L (IV), forming a covalent or non-covalent bond
     between (IV) and the substrate B1 or forming a covalent bond between B1
     and the linker to form a conjugate B-L followed by conjugation with the
     monomer, and
          (5) a kit for preparing a radiopharmaceutical comprising (A1).
          Bla = a phospholipid group of formula (ii);
          M = alkaline or alkaline earth metal cation;
          R1, R2 = 12-20C linear chain optionally interrupted by CO or O, and
          X2 = H, CH2CH2NH2, CH2CH(NH3+)-COO-, CH2CH(OH)CH2OH or a group of
     formula (iii).
          ACTIVITY - Cytostatic; Antiangiogenetic.
          MECHANISM OF ACTION - Vascular endothelial growth factor binding
     receptor transmembrane glycoprotein (NP-1) binder.
          USE - Used for targeting endothelial cells, tumor cells or other
     cells which express NP-1, for inhibiting angiogenesis, for ultrasound
     imaging, staging a tumor, screening at least one targeted ultrasound
     contrast agent for the ability to target endothelial cells, tumor cells or
     other cells which express NP-1, for the therapeutic delivery in vivo of a
     bioactive agent and for delivering desired nucleic acids to endothelial
     cells, tumor cells or other cells which express NP-1 (all claimed). The
     composition is also useful for visualization therapy or radiotherapy of
     endothelial cells.
          ADVANTAGE - (A1) can be used with or without a detectable moiety for
     any of the imaging modalities.
     Dwg.0/4
     CPI
    AB; GI; DCN
     CPI: A12-V01; A12-V03C2; B01-D02; B03-H; B04-B01B; B04-C01A; B04-C02;
          B04-C03; B04-D01; B04-J02; B05-A03B; B05-A04; B05-B01P; B05-B02C;
          B05-C08; B10-A07; B10-B02J; B10-B04B; B10-C02; B10-H02B; B12-K04C1;
          B14-F01D; B14-H01; K08-X; K09-B; K09-E
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        *32* DCN: 0097-34701-T; 0097-34701-M; 0097-34701-N
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        *39* DCN: RA0120-K; RA0120-T; RA0120-Q; RA0120-M
        *40* DCN: RA01IK-K; RA01IK-T; RA01IK-Q; RA01IK-M
        *41* DCN: RA01PM-K; RA01PM-T; RA01PM-Q; RA01PM-M
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        *43* DCN: RA0121-K; RA0121-T; RA0121-Q; RA0121-M
        *44* DCN: RA04V6-K; RA04V6-T; RA04V6-Q; RA04V6-M
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        *47* DCN: 0097-34703-K; 0097-34703-T; 0097-34703-Q; 0097-34703-M;
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    M2
        *04* DCN: R09617-K; R09617-T; R09617-Q; R09617-M; R10728-K; R10728-T;
                   R10728-Q; R10728-M
    M2
        *05* DCN: R01065-K; R01065-T; R01065-Q; R01065-M
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FS

FA

L4

M2 *06* DCN: RAOICL-K; RAOICL-T; RAOICL-Q; RAOICL-M

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*07* DCN: RA11FY-K; RA11FY-T; RA11FY-Q; RA11FY-M
    *08* DCN: RA1AGG-K; RA1AGG-T; RA1AGG-Q; RA1AGG-M
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    *10* DCN: R00104-K; R00104-T; R00104-Q; R00104-M; R04091-K; R04091-T;
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    *11* DCN: R00116-K; R00116-T; R00116-Q; R00116-M; R04750-K; R04750-T;
M2
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    *12* DCN: R00114-K; R00114-T; R00114-Q; R00114-M; R04738-K; R04738-T;
M2
              R04738-Q; R04738-M
    *13* DCN: R00100-K; R00100-T; R00100-Q; R00100-M; R17997-K; R17997-T;
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    *14* DCN: R06639-K; R06639-T; R06639-Q; R06639-M
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   *21* DCN: R16329-K; R16329-T; R16329-Q; R16329-M
   *22* DCN: R16328-K; R16328-T; R16328-Q; R16328-M
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*24* DCN: R01779-K; R01779-T; R01779-Q; R01779-M
M2
    *25* DCN: R03186-K; R03186-T; R03186-Q; R03186-M
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    *29* DCN: R18066-K; R18066-T; R18066-Q; R18066-M
    *30* DCN: RAAXL7-K; RAAXL7-T; RAAXL7-Q; RAAXL7-M
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    *33* DCN: R11954-K; R11954-T; R11954-Q; R11954-M
   *34* DCN: R13257-K; R13257-T; R13257-Q; R13257-M
   *35* DCN: R00148-K; R00148-T; R00148-Q; R00148-M
M5
    *36* DCN: RAAXKP-K; RAAXKP-T; RAAXKP-Q; RAAXKP-M
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